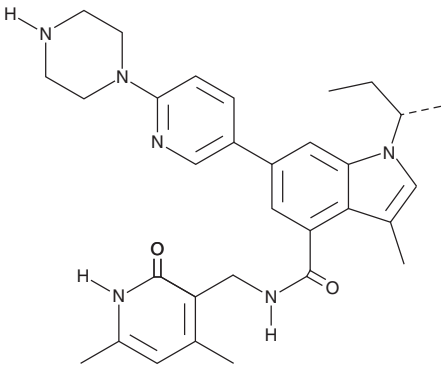
PRODUCT INFORMATION

GSK126

Item No. 15415

CAS Registry No.:	1346574-57-9
Formal Name:	N-[(1,2-dihydro-4,6-dimethyl-2-oxo-3-pyridinyl)methyl]-3-methyl-1-[(1S)-1-methylpropyl]-6-[6-(1-piperazinyl)-3-pyridinyl]-1H-indole-4-carboxamide
MF:	$C_{31}H_{38}N_6O_2$
FW:	526.7
Purity:	≥98%
UV/Vis.:	λ_{max}: 235, 283 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

GSK126 is supplied as a crystalline solid. A stock solution may be made by dissolving the GSK126 in the solvent of choice, which should be purged with an inert gas. GSK126 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of GSK126 in these solvents is approximately 2, 15, and 25 mg/ml, respectively.

GSK126 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, GSK126 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. GSK126 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

The histone H3 lysine 27 (H3K27) methyltransferase EZH2 plays an important role in regulating gene expression, and its aberrant activity is linked to the onset and progression of cancer.[1] GSK126 is a selective, S-adenosyl-methionine-competitive small molecule inhibitor of EZH2 methyltransferase activity (K_i = 0.57 nM; IC_{50} = 9.9 nM *versus* that of EZH1: K_i = 89 nM; IC_{50} = 680 nM).[2] It is more than 1,000-fold selective for EZH2 over other histone methyltranferases, including both SET-domain-containing and non-SET-domain-containing methyltransferases.[2] At concentrations of 7-252 nM, it has been shown to inhibit global H3K27 trimethylation levels and to reactivate silenced PRC2 target genes.[2] Furthermore, GSK126 can inhibit the proliferation of EZH2 mutant DLBCL cell lines (IC_{50} = 28-61 nM) as well as the growth of EZH2 mutant DLBCL xenografts in mice receiving a daily dose of 50 mg/kg.[2]

References

1. Simon, J.A. and Lange, C.A. Roles of the EZH2 histone methyltransferase in cancer epigenetics. *Mutat. Res.* **647**, 21-29 (2008).
2. McCabe, M.T., Ott, H.M., Ganji, G., *et al.* EZH2 inhibition as a therapeutic strategy for lymphoma with EZH2-activating mutations. *Nature* **492(7427)**, 108-112 (2012).

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